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肿柄菊的化学成分

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Chemical Constituents from *Tithonia diversifolia*

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Tithonia diversifolia（Hemsl.）A. Gray（Compositae）is an American plant which has become naturalization in the south of China. In Yunnan，it is mainly distributed on small hills of torrid zone with an altitude from 500 to 1600 meters above sea level. The leaves have been used as an agent for subduing swelling，dissolving lumps and treating enteritis and gastritis in local folk medicine（云南省药材公司，1993）. Previous report showed that *T. diversifolia* was rich in sesquiterpene lactones（Raghwendra *et al*，1976）. However，the plant distributed in Yunnan has not been studied yet. As a continuation of our phytochemical investigations on the biological active constituents，we recently investigated the chemical constituents of *T. diversifolia* collected in Yuanyang County of Yunnan，which led to the isolation of two sesquiterpene lactones as well as 3，5－di－*O*－caffeoylquinic acid.

Results and Discussion

Compound 1 was obtained as amorphous powder and its MS and NMR spectra indicated molecular formula of $C_{19}H_{28}O_7$，suggesting four methyls，three methylenes，six methines，two quaternary carbons，two ketonic carbon and two olefinic carbons（terminal double bond）. Six degrees of unsaturation of **1** revealed that **1** had three rings. The *exo*－methylene group and one of the carbonyl group should be conjugated as evidenced by characteristic UV and IR absorptions. Since the presence of an isobutyryl group was clearly observed from the 2D NMR spectra and EIMS peaks of 297（［M－COCH

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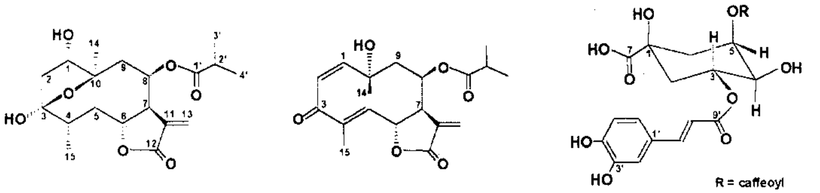
$(CH_3)_2]^+$) and 280 ([M – HOOCCH $(CH_3)_2]^+$), **1** was presumed to possess sesquiterpene skeleton.



1 2 3

From the $^1H-^1H$ COSY and HMQC spectra of **1**, the existence of fragments – $CHCH_2$ – (C – 1 to C – 2) and – (CH_3) $CHCH_2CHCHCHCH_2$ – (Me – 15, C – 4 to C – 9) were clearly evident. HMBC experiment exhibited that **1** was a sesquiterpene possessing a ten – membered ring, and there was an isobutyryl group at C – 8 and two hydroxyl groups at C – 1 and C – 3 respectively. Moreover, between C – 6 and C – 7 formed an extra lactone ring which include five members, and C – 3 and C – 10 was connected by an oxo bridge (Figure 1). Comparing all the spectral data of **1** with those of tagitinin A, **1** was identical to the latter. Therefore, **1** was determined to be tagitinin A (Raghwendra *et al*, 1976a; Raghwendra *et al*, 1976b; Sarma *et al*, 1987).

Inspection of EIMS and NMR spectra suggested that **2** has a molecular formula of $C_{19}H_{24}O_6$ and is also a sesquiterpene. Its basic skeleton was very similar to that of **1** except for two more double bonds between C – 1 and C – 2 and C – 4 and C – 5. Analysis of HMBC spectrum of **2** led to a conclusion that **2** was tagitinin C, which was further verified by all the spectral data of **2** being in quite agreement with those of the latter. Thus, **2** was deduced as tagitinin C (Raghwendra *et al*, 1977; Baruah *et al*, 1979).

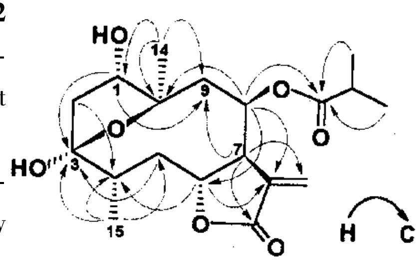


Fig. 1 The key HMBC correlations of **1**

Table 1 ^{13}C NMR data of tagitinin A (**1**) and C (**2**) in C_5D_5N (100.6 MHz, δ)

C	1	2	C	1	2
1	78.9 d	162.2 d	11	138.7 s	138.9 s
2	48.1 t	130.2 d	12	170.1 s	170.3 s
3	106.3 s	197.1 s	13	120.7 t	123.5 t
4	45.1 d	138.9 s	14	25.4 q	29.1 q
5	39.0 t	137.8 d	15	19.4 q	19.7 q
6	82.2 d	76.7 d	1′	176.1 s	175.8 s
7	48.4 d	47.5 d	2′	34.4 d	34.5 d
8	71.0 d	75.3 d	3′	18.9 q	19.0 q
9	35.9 t	48.9 t	4′	18.7 q	18.9 q
10	81.6 s	71.4 s			

Spectral comparison of **3** and 3，5 – di – *O* – caffeoylquinic acid indicated they were all the same compound，which was also confirmed by comparing **3** with the authentic sample of the latter on co – TLC（Wang *et al*，1992）.

Experinental

General Optical rotations were measured on a Jasco Dip – 369 Digital polarimeter. UV spectra were determined in MeOH，employing a Shimadzu UV – 210 A instrument. IR spectra were obtained on a Bio – Rad FTS – 135 spectrometer with KBr pellets. NMR spectra were recorded on Bruker AM – 400 and DRX – 500 instruments with TMS as internal standard and pyridine – d_5 as solvent. EI and FAB MS were carried out on a VG Auto Spec – 3000 spectrometer at 70 eV.

Plant material The leaves of *Tithonia diversifolia*（Hemsl.）A. Gray were collected in Yuanyang County of Yunnan Province in December of 1997. It was authenticated by Prof. Zhong – Wen Lin at Kunming Institute of Botany，Chinese Academy of Sciences，where a voucher specimen is deposited.

Extraction and isolation Dried and powdered leaves（2.4 kg）were extracted with 70% Me_2CO（25 L × 3）. The solution was concentrated to about 3000 mL and then submitted to DM – 130 column and eluted with solvents of H_2O，60% MeOH and 70% Me_2CO respectively. The fraction of 60% MeOH was evaporated in vacuum to give a residue（40 g）which was then chromatographed on a Sephadex LH – 20 column and eluted with H_2O containing increasing amounts of MeOH. The fractions were combined by monitoring with TLC. Appropriate fractions were further submitted to MCI – gel CHP – 20P and Si gel column and eluted with proper solvents finally yielding three compounds **1**（1.02 g），**2**（48 mg）and **3**（12 mg）.

Tagitinin A（1），$C_{19}H_{28}O_7$，was obtained as amorphous powder；$[\alpha]_D^{22}$ – 160°（c 0.86，MeOH）；UV（MeOH）λ_{max}（log ε）nm：213（4.06）；IR ν_{max}^{KBr} cm^{-1}：3462（br），2975，2938，2880，1742（br），1658，1461，1389，1318，1264，1237，1198，1156，1107，1068，1027，1000，983，961，928，890，818 cm^{-1}；EIMS *m/z*（%）：368（6）$[M]^+$，350（6）$[M-H_2O]^+$，325（1）$[M-CH(CH_3)_2]^+$，297（2）$[M-COCH(CH_3)_2]^+$，280（20）$[M-HOOCCH(CH_3)_2]^+$，262（33）$[M-HOOCCH(CH_3)_2-H_2O]^+$，244（11），237（16），219（17），211（56），191（22），181（36），165（38），147（36），121（38），97（43），79（26），71（100）；^1H NMR（C_5D_5N，400 MHz）δ：4.41（1H，overlapped，H – 1β），2.78（1H，dd，J = 9.12，13.56 Hz，H – 2β），2.45（1H，overlapped，H – 2α），2.45（1H，overlapped，H – 4β），2.65（1H，m，H – 5α），2.01（1H，dd – like，J = 12.64，2.8 Hz，H – 5β），4.88（1H，m，H – 6β），4.44（1H，overlapped，H – 7α），5.98（1H，m，H – 8α），2.45（1H，overlapped，H – 9β），2.27（1H，dd，J = 11.74，14.28 Hz，H – 9α），6.41（1H，s，H – 13a），5.72（1H，s，H – 13b），1.48（3H，s，Me – 14），1.28（3H，d，J = 6.92 Hz，Me – 15），2.45（1H，overlapped，H – 2′），1.06（3H，d，J = 6. 80 Hz，Me – 3′），1.05（3H，d，J = 6.80 Hz，Me – 4′）. ^{13}C NMR spectral data，see Table 1.

Tagitinin C (2), $C_{19}H_{24}O_6$, amorphous powder; $[\alpha]_D^{22}$ $-202°$ (c 0.97, MeOH); UV (MeOH) λ_{max} (log ε) nm: 214 (4.22), 247 (4.04); IR ν_{max}^{KBr} cm^{-1}: 3467 (br), 2977, 2937, 2880, 1770, 1736, 1657, 1469, 1458, 1388, 1375, 1341, 1281, 1257, 1235, 1194, 1153, 1133, 1070, 1044, 993, 948, 871, 818 cm^{-1}; EIMS *m/z* (%): 348 (6) $[M]^+$, 330 (2) $[M-H_2O]^+$, 305 (4) $[M-CH(CH_3)_2]^+$, 277 (26) $[M-COCH(CH_3)_2]^+$, 260 (100) $[M-HOOCCH(CH_3)_2]^+$, 242 (25) $[M-HOOCCH(CH_3)_2-H_2O]^+$, 232 (85), 217 (94), 189 (63), 175 (34), 149 (94), 135 (42), 95 (44), 71 (90); ^1H NMR (C_5D_5N, 400 MHz) δ: 7.37 (1H, d, J = 17.14 Hz, H-1), 6.60 (1H, d, J = 17.14 Hz, H-2), 5.99 (1H, d, J = 11.60 Hz, H-5), 5.96 (1H, br d, J = 11.60 Hz, H-6β), 4.03 (1H, br s, H-7α), 5.90 (1H, overlapped, H-8α), 2.67 (1H, dd, J = 6.36, 13.72 Hz, H-9β), 2.29 (1H, dd, J = 10.16, 13.72 Hz, H-9α), 6.40 (1H, s, H-13a), 5.80 (1H, s, H-13b), 1.57 (3H, s, Me-14), 1.94 (3H, s, Me-15), 2.49 (1H, m, H-2′), 1.05 (3H, d, J = 6.20 Hz, Me-3′), 1.03 (3H, d, J = 6.20 Hz, Me-4′). ^{13}C NMR spectral data, see Table 1.

3,5-Di-*O*-caffeoylquinic acid (3), $C_{25}H_{24}O_{12}$, yellow amorphous powder; negative FAB-MS *m/z* (%): 515 (100) $[M-H]^-$, 353 (57) $[M-H-C_9H_6O_3$ (caffeoyl group $-$ H)$]^-$, 325 (40) $[M-H-C_9H_6O_3-CO]^-$, 311 (18), 279 (44), 265 (5), 191 (49) $[M-H-2\times C_9H_6O_3]^-$, 173 (34) $[M-H-2\times C_9H_6O_3-H_2O]^-$, 155 (5) $[M-H-2\times C_9H_6O_3-H_2O-CO]^-$, 134 (13), 97 (8), 80 (13); ^1H NMR (C_5D_5N, 400 MHz) δ: 2.93-2.76 (4H, overlapped, H_2-2 and H_2-6), 6.42 (1H, br dd, J = 8.44, 2.80 Hz, H-3β), 4.99 (1H, br. d, J = 8.44 Hz, H-4α), 5.79 (1H, br s, H-5α), 7.49 (2H, d, J = 2.20 Hz, H_2-2′ and 2″), 7.05 (2H, d, J = 7.04 Hz, H_2-5′ and 5″), 7.16 (2H, dd, J = 7.04, 2.20 Hz, H_2-6′ and 6″), 7.99 (2H, d, J = 15.60 Hz, H_2-7′ and 7″), 6.58 (2H, d, J = 15.60 Hz, H_2-8′ and 8″); ^{13}C NMR (C_5D_5N, 100.6 MHz) δ: 76.3 (s, C-1), 40.1 (t, C-2), 69.2 (d, C-3), 69.0 (d, C-4), 69.0 (d, C-5), 39.0 (t, C-6), 177.5 (s, C-7), 127.0 (s, C-1′, 1″), 116.0 (d, C-2′, 2″), 146.7 (s, C-3′, 3″), 150.6 (s, C-4′, 4″), 116.8 (d, C-5′, 5″), 122.3 (d, C-6′, 6″), 147.7 (d, C-7′, 7″), 115.4 (d, C-8″, 8″), 167.5 (s, C-9′), 167.1 (s, C-9″).

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